

## Book Review

*Evolution: A View from the 21st Century* by James A. Shapiro. Upper Saddle River, NJ: FT Press, 2011. 253+xviii pp. US \$39.44 hb.

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*Evolution: A View from the 21st Century*, written by an eminent microbiologist–bacterial molecular geneticist, is an ambitious book. It has something novel and highly interesting to say about evolution and it deserves to be widely read.

Nevertheless, I have found doing this review a difficult exercise. In the interest of “full disclosure,” I should say that the author, Jim Shapiro, is a friend with whom I have previously discussed these ideas. (I had not, however, known about the book until it was published.) Friends, however, do not always agree and he and I have differed about some of his ideas. Nor have those disagreements been dispelled by my reading the book. In particular, I think that there is an alternative interpretation of some of the phenomena presented and cited here as providing support for the central thesis. In addition, I regard one core proposition, though only explicitly stated at the end and then partially hedged, as, simply, wrong. Hence, although I strongly recommend the book and hope that it is widely read and discussed, I cannot equivalently endorse its big idea or, at least, not all of it. In this review, I will first describe the contents of the book and its central thesis and will then try to explain where the problems, in my opinion, reside.

A few words first, however, about the author and his pathway into evolution from bacterial molecular genetics, might be appropriate. Jim Shapiro was, as a postdoc in Jonathan Beckwith's lab in 1969, the first person to purify a small set of protein-coding genes, those of the *lac* operon (which had been imbedded in a much larger set of phage genes within transducing phages). The strategy was brilliant but was not applicable to most genes, hence, it was superseded by the more general cloning techniques for specific genes that came to the fore in the early 1970s. Nevertheless, it was a milestone in the development of the modern (post-60s) form of molecular biology, involving DNA sequence isolation and characterization. Even more significantly, Jim had, as a postdoc with Francois Jacob, the preceding year, discovered that certain mutations in *Escherichia coli* were due to insertions of bacterial transposable elements, the so-called insertion sequence (IS) elements. The discovery immediately

made geneticists aware that the transposable element phenomenon, discovered by Barbara McClintock in maize two decades earlier but dismissed as an oddity by most geneticists, was, almost certainly, a general one, with major implications for mechanisms of gene control, biological development, and evolution (Bukhari et al. 1977). That work eventually led on to a 12-year friendship between Jim and Barbara McClintock, which lasted until her death. In that friendship and exchange of ideas lay the seeds of Jim's interest in evolution—the major focus of McClintock's attention in the last decades of her life—and, ultimately, in the thesis developed in this book.

The key goal of this book is to demonstrate that a central premise of Darwinian evolution is incorrect and to spell out the implications of that conclusion for evolutionary theory. The Darwinian premise is that genetic variations—“mutations” including chromosomal breaks and rearrangements) in current terminology but “hereditary variations” in Darwin's—occur “randomly,” that is, irrespectively of environmental conditions and adaptive “need.” (Darwin actually equivocated somewhat on this point, at times endorsing the inheritance of acquired characteristics, but he seemed aware that the strong form of his theory required that variations arise by chance, i.e., without respect to future utility, hence randomly.) This central plank of classic Darwinian evolution is also embedded, according to Jim and several others, in a more recent formulation, namely Francis Crick's “central dogma,” first stated in 1958, and reiterated and (basically reaffirmed) by Crick in 1970. This is the idea that “information” flows one-way from nucleic acids (DNA and RNA) to proteins and never in the reverse direction. From this, Jim argues that it is tantamount to the statement that environmental influences never influence DNA structure and information content; the flow of “instruction” is always one-way, outwards from DNA to proteins and thence to biological properties. (His formulation of this view is that it treats the genome as a “read only memory” storage system.)

Whether that extrapolation from Crick's statement is truly fair is something best left to historians of science. In neither statement, to my eye, was Crick explicitly considering the kinds of organismal response that can alter genomic

sequences in response to environmental perturbation, the focus of this book. (As for the ability of some environmental agents to alter DNA, he was certainly aware, for instance, that mutagens can do so.) Crick was discussing solely the direction of sequence information flow between the two classes of macromolecules and his specific conclusion is still valid: nucleic acid sequence information can be read into proteins or copied into each other (DNA → RNA or RNA → DNA) but protein sequences cannot be reverse-read into nucleic acid sequences. (The degeneracy of the genetic code, discovered subsequently to Crick's original formulation, clinches the argument.) Nevertheless, leaving aside that question of interpretation and historical justice, the starting point of Jim's critique is also true. Contemporary evolutionary theory posits the independence of newly arising mutations from any future potential employment by the organism, hence randomly. In the classical formulation, evolution has no "foresight" with respect to the production of new genetic variants.

A major part of the book, about two-thirds, is devoting to demonstrating that this key tenet of the Modern Synthesis is false. It documents a great deal of genetic change that is not "random," in the above sense, but is created by cellular systems often in response to environmental challenges. Most of this material is covered in the longest section of the book, "The genome as a read-write (RW) storage system," while additional facts about genome remodeling in response to environmental influences are in the penultimate section, "Evolutionary lessons from molecular genetics and genome sequencing." (The last section of the book reviews the main lines of evidence and summarizes the key conclusions.)

Altogether, the evidence marshaled in the book for genomic responses and remodeling in response to environmental and developmental cues is a long and impressive one. It includes such phenomena as: the gene rearrangements essential to and ubiquitous within the mammalian adaptive immune system, the restructuring of ciliate macronuclei, changes within the genomes of sporulating bacteria, the yeast mating-type system, massive genome "restructuring" during plant hybridization, hybrid dysgenesis in *Drosophila*, a host of transposon- and retrotransposon-mediated genetic changes in plants and animals, and much more. In addition, the nature and potential importance of stable epigenetic (chromatin-based) changes, as a complement to and distinctly different from pure genetic (DNA sequence) changes, is explored. The information in the text is supplemented by a large collection of online supplementary material, an unusual feature for a book aimed principally at the general reader and a highly valuable one, especially for biologist readers. Indeed, the book, with its online supplements, is a treasure trove of information. (There is, however, a small problem in retrieving some of the information: the bibliographic system in the printed text simply lists references in order of appearance, making it difficult to check whether a particular author or article has been cited. This problem is partly corrected by the online referencing sys-

tem, which can be found at <http://shapiro.bsd.uchicago.edu/evolution21.shtml>.)

The general argument of the book, buttressed by all these examples—that genomes can be highly responsive to environmental influences, becoming "reformatted" to greater or lesser extent—is clearly important. It is not wholly new, however. It was made previously by Caporale (2003) and by Jablonka and Lamb (1995, 2005). Furthermore, the omission of any mention of Miroslav Radman's work on DNA repair, induced mutations and organismal "evolvability" (Radman et al. 1999), is surprising. Yet, the entire set of evidence for genome restructuring in response to environmental signals is more extensively documented than in earlier accounts and is, correspondingly, made even more compellingly by this book.

Furthermore, the general phenomenon is given a name here, namely "natural genetic engineering," defined as the ability of cells to alter their genomes in response to environmental challenge. This idea and the term have been given previous exposure in articles by Jim, the earliest in 1992, but the idea is more fully fleshed out and defended here. It might seem, however, that the term itself is problematical. Can there be "engineering" without an engineer? And, if so, what does the engineering? The text makes clear, however, that the term implies no external agent. It designates an inherent set of cellular capabilities for such genome restructuring. The cell is thus its own agent, its own engineer.

The argument is thought-provoking and the range of findings described, to support it, should be of interest to all cellular, developmental, and evolutionary biologists. There are, however, some counterarguments to be made to the general thesis or, at least, caveats to be registered. The first concerns transmissibility of the induced genetic changes to future generations. Many of the phenomena involving multicellular organisms discussed extensively in the book involve DNA arrangements within the somatic cells and nuclei of those organisms. Such soma-only processes, such as the mammalian adaptive immune system and the degradation of ciliate macronuclei, are, indeed, examples of cellular "genetic engineering" and have direct survival value for the individual cell or organism. Being purely somatic, however, they are not transmitted to the next generation and hence lack "direct" evolutionary potential. "Indirect" consequences of those genomic changes, affecting survival and ultimately "fitness," are, of course, a different matter but those effects must involve the operation of natural selection, a subject that receives surprising treatment in this book, as discussed below. (In contrast to the soma-only genomic reformattings, several transposable elements, such as the P-elements of *Drosophila*, mediate genomic changes solely in the germ line, and these clearly do have evolutionary potential.)

Second, among the genomic remodeling events described here that can be transmitted across generations,

none relate directly to developmental/morphological evolution, the main focus of traditional evolutionary biology. Instead, many of the phenomena listed that possess such direct evolutionary potential take place within the context of host and parasite “arms races.” In these, the new variants that are generated, by either host or parasite, are not limited to those that are directly tailored to the particular situation. Instead, a large set of new variants is generated through a general increase in the rate of gene sequence change, and of these, only a few directly meet the specific environmental challenge. This scattershot generation of new variants appears to be the case in situations as diverse as the so-called adaptive mutation response in *E. coli*, the DNA error-prone repair processes described by Radman et al. (1999) (these latter two not involving arms races) and the generation of antigen diversity in malarial trypanosomes. Hence, there are (as yet) no cases of “precisely targeted” evoked genetic variation, to create specific new gene alleles, in response to environmental hazards. Thus, environmental influences can evoke particular classes of genetic change, but, to date, only a few cases of specific genes being remodeled in specific ways to meet an adaptive challenge have been documented. (The *Salmonella* antigen-switching system and the yeast mating-type system are in this category, if “adaptive challenge” is interpreted broadly.)

The arms race analogy may also be of relevance to those cases of genomic change in response to transposable elements and retrotransposon activities that comprise a large percentage of the total number of cited cases (see Table II.7, pp. 70–74). Described in this book as part of the natural genetic engineering machinery that the cell employs for its own purposes (i.e., for its descendants), those activities can, instead, be interpreted as reflecting their original genomic parasitic character (Ryan 2009; Wilkins 2010). In this view, occasional variants/genomic changes produced by these elements that have adaptive value for the host are an accidental by-product of the process of retrotransposon activation while the activation events themselves, which are often triggered by environmental stresses, are part of the mobile elements’ survival repertoires. To make this case, however, is not to deny the frequent incorporation, over evolutionary time spans, of retrotransposons in the functional regulatory machinery of the cell, a phenomenon that is well described in this book. Such incorporation reflects the long-term “domestication” of such elements and their subsequent conscription into host functions. Accordingly, Frank Ryan, the author of *Violution* (Ryan 2009), favors the term “symbionts” for such elements rather than parasites; his term implicitly acknowledges the often beneficial (though evolved) roles of retrotransposons. Yet, to see most retrotransposon activations as something evolved for the benefit of these elements rather than serving as something, initially and primarily, for the host’s benefit is a very different perspective from that of the natural genetic engineering concept.

My final disagreement with Jim’s general argument concerns a truly fundamental point, however: the dismissal of natural selection as a shaping force in evolution. Thus, it is stated, at the very start of the book (top of p. 1): “Innovation, not selection, is the critical issue in evolutionary change. Without variation and novelty, selection has nothing to act upon.” Although all evolutionists would agree wholeheartedly with the second sentence, most would reject the first. The matter of selection is then virtually ignored until the final section of the book. There we read, as one of nine bullet points that summarize the core message: “The role of selection is to eliminate evolutionary novelties that prove to be non-functional and interfere with adaptive needs. Selection operates as a *purifying but not creative force* [emphasis added].”

I cannot imagine many evolutionary biologists subscribing to that position. The objections to it come from both genetic arguments and paleontological data. Take the genetic considerations first. In microbes, the number of steps between a genetic change and its phenotypic consequences is usually small, often being simply the function of an altered encoded protein. One might say that, in general, within prokaryotes, the “genotype–phenotype distance” is short. The consequence is a fairly direct and predictable biological consequence, whose selective consequences (favorable or unfavorable) are often easy to predict. In contrast, in complex multicellular organisms, the genotype–phenotype distance is large, the effects of most genetic changes being transmitted through complex genetic networks and cellular changes. These, which can be diagrammed as a linear sequence (though often embedded within larger branching networks), constitute a large sequence of steps, one that eventuates in morphological change. Furthermore, the genetic change often has pleiotropic consequences. The net result of all these complexities is that the biological consequences of a genetic (or stable epigenetic) change are often both indirect and mixed. In such situations, there will be trade-offs between biological fitness gains and losses for each resultant change. Natural selection must comprise an important part of the process that either filters out or amplifies the effect of most such changes.

The arguments from paleontological evidence for the importance of natural selection largely concern the observed long-term trends of morphological change, which are visible in many lineages. It is hard to imagine what else but natural selection could be responsible for such trends, unless one invokes supernatural or mystical forces such as the long popular but ultimately discredited force of “orthogenesis.” For a detailed consideration of these cases and the role of natural selection in shaping morphologies of organisms over long time spans, there is no better general treatment than the classic book of Simpson (1971).

Finally, with respect to this issue of selection, one might add that, in terms of Jim’s particular thesis, it is hard to understand how cells could have the very capacities for natural

genetic engineering attributed to them without those capacities having been evolved, in some manner and over long evolutionary spans, by natural selection. The evolution of such capabilities, favoring the process of evolvability (the capacity to give rise to new properties), is a fascinating subject, though mentioned explicitly only once in the book, and deserves more attention than it has traditionally received. Again, the only alternative for the origination of these capabilities, if one discards natural selection as the generative agent, is some supranatural force, a position that I am certain is not being advocated here.

On the other hand, perhaps, the rejection of the creative role of natural selection in transforming populations is not as complete as the earlier statements suggest. The next to last bullet point, in the summation of conclusions (p. 144), states: "Successful evolutionary inventions are subject to amplification, reuse, and adaptation to new functions in response to successive ecological changes." To me, that reads like a classic statement for the role of directional selection in promoting evolutionary change via the transformation of the genetic structure of a population. Certainly, the spread of antibiotic resistance, discussed at length in the book, would appear to be an archetypal instance of natural selection—albeit one based on a highly nonclassical form of genetic variation—as, indeed, it is so regarded by most biologists.

Yet, the book's contention that natural selection's importance for evolution has been hugely overstated represents a point of view that has a growing set of adherents. (A few months ago, I was amazed to hear it expressed, in the strongest terms, from another highly eminent microbiologist.) My impression is that evolutionary biology is increasingly separating into two camps, divided over just this question. On the one hand are the population geneticists and evolutionary biologists who continue to believe that selection has a "creative" and crucial role in evolution, and on the other, there is a growing body of scientists (largely those who have come into evolution from molecular biology, developmental biology or developmental genetics, and microbiology) who reject it. In contrast to Victorian scientists who regarded Darwinian natural selection as "incapable" of creating high degrees of biological complexity, the modern sceptics tend to regard it as of "trivial" importance: the "right" variant for the right place and time arises and, presto, the population changes! The two contemporary groups, divided over this point, are not so much talking past each another as ignoring one another. This

cannot be a constructive situation though whether it has the makings of a full-fledged Kuhnian paradigm crisis is too soon to tell.

Let me end on a positive note. Jim Shapiro has made a well-documented case against the sufficiency of random mutations (arising irrespective of potential need) as the source material for genetic variation and has discussed a wide variety of mechanisms by means of which, in some degree, genetic change is evoked in direct response to environmental challenge. There is a plethora of information that he marshals, both within the printed book and in the online material and these specific findings and the general phenomenon they illustrate deserve far more attention from evolutionary biologists than they have so far received. A particular challenge now is to find out how much evolutionarily significant genetic change is evoked in response to specific environmental changes and what kinds of change they comprise.

Evolutionary biology is clearly experiencing interesting times. Perhaps, however, it is best that way. At least, it makes for the prospect of a more interesting future than the equivalent, to use a Victorian-era image, of a lot of people somnolently nodding their agreement ("yes, yes, quite so") over their after-dinner glasses of port. That latter characterization is not too far off how the field of evolutionary biology appeared for several decades in the mid- to late-20th century. Jim Shapiro's book provides a highly useful contribution to the more interesting ferment in evolutionary thinking that apparently lies ahead.

## Literature Cited

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